

SEQUENCE LISTING

<110> Clausen, Henrik Bennett, Eric P.

<120> METHODS TO IDENTIFY AGENTS MODULATING FUNCTIONS OF POLYPEPTIDE GALNAC-TRANSFERASES, PHARMACEUTICAL COMPOSITIONS COMPRISING SUCH AGENTS AND THE USE OF SUCH AGENTS FOR PREPARING MEDICAMENTS

- <130> 04305/100H154-US2
- <150> US 60/425,204
- <151> 2002-11-08
- <150> PCT/DK03/00763
- <151> 2003-11-07
- <160> 127
- <170> PatentIn version 3.1
- <210> 1
- <211> 20
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- <213> Artificial Sequence
- <220>
- <223> synthetic peptide
- <400> 1

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Ala Pro Pro Ala 20

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Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro 1 10 15

Ala Pro Gly Ser Thr Ala Pro Pro 20

- <210> 3
- <211> 167
- <212> PRT
- <213> Homo sapiens

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<210> 4

<211> 164

<212> PRT

<213> Homo sapiens

<400> 4

Tyr Gly Asn Ile Gln Ser Arg Leu Glu Leu Arg Lys Lys Leu Ser Cys $1 \hspace{1cm} 10 \hspace{1cm} 15$

Lys Pro Phe Lys Trp Tyr Leu Glu Asn Val Tyr Pro Glu Leu Arg Val 20 25 30

Pro Asp His Gln Asp Ile Ala Phe Gly Ala Leu Gln Gln Gly Thr Asn 35 40 45

Cys Leu Asp Thr Leu Gly His Phe Ala Asp Gly Val Val Gly Val Tyr

50 55

60

Glu Cys His Asn Ala Gly Gly Asn Gln Glu Trp Ala Leu Thr Lys Glu 65 70 75 80

Lys Ser Val Lys His Met Asp Leu Cys Leu Thr Val Val Asp Arg Ala 85 90 95

Pro Gly Ser Leu Ile Lys Leu Gln Gly Cys Arg Glu Asn Asp Ser Arg 100 105 110

Gln Lys Trp Glu Gln Ile Glu Gly Asn Ser Lys Leu Arg His Val Gly 115 120 125

Ser Asn Leu Cys Leu Asp Ser Arg Thr Ala Lys Ser Gly Gly Leu Ser 130 140

Val Glu Val Cys Gly Pro Ala Leu Ser Gln Gln Trp Lys Phe Thr Leu 145 150 155 160

Asn Leu Gln Gln

<210> 5

<211> 167

<213> Homo sapiens

<400> 5

Phe Gly Asp Leu Ser Lys Arg Phe Glu Ile Lys His Arg Leu Arg Cys 1 10 15

Lys Asn Phe Thr Trp Tyr Leu Asn Asn Ile Tyr Pro Glu Val Tyr Val 20 25 30

Pro Asp Leu Asn Pro Val Ile Ser Gly Tyr Ile Lys Ser Val Gly Gln 35 40 45

Pro Leu Cys Leu Asp Val Gly Glu Asn Asn Gln Gly Gly Lys Pro Leu 50 60

Ile Met Tyr Thr Cys His Gly Leu Gly Gly Asn Gln Tyr Phe Glu Tyr 65 70 75 80

Ser Ala Gln His Glu Ile Arg His Asn Ile Gln Lys Glu Leu Cys Leu 85 90 95

His Ala Ala Gln Gly Leu Val Gln Leu Lys Ala Cys Thr Tyr Lys Gly 100 105 110

His Lys Thr Val Val Thr Gly Glu Gln Ile Trp Glu Ile Gln Lys Asp 115 120 125

Gln Leu Leu Tyr Asn Pro Phe Leu Lys Met Cys Leu Ser Ala Asn Gly 130 135 140

Glu His Pro Ser Leu Val Ser Cys Asn Pro Ser Asp Pro Leu Gln Lys 145 150 155 160

Trp Ile Leu Ser Gln Asn Asp 165

<210> 6

<211> 174

<212> PRT

<213> Homo sapiens

<400> 6

Ala Tyr Gly Asp Ile Ser Glu Arg Lys Leu Leu Arg Glu Arg Leu Arg 1 10 15

Cys Lys Ser Phe Asp Trp Tyr Leu Lys Asn Val Phe Pro Asn Leu His 20 25 30

Val Pro Glu Asp Arg Pro Gly Trp His Gly Ala Ile Arg Ser Arg Gly 35 40 45

Ile Ser Ser Glu Cys Leu Asp Tyr Asn Ser Pro Asp Asn Asn Pro Thr 50 60

Gly Ala Asn Leu Ser Leu Phe Gly Cys His Gly Gln Gly Gly Asn Gln 65 70 75 80

Phe Phe Glu Tyr Thr Ser Asn Lys Glu Ile Arg Phe Asn Ser Val Thr 85 90 95

Glu Leu Cys Ala Glu Val Pro Glu Gln Lys Asn Tyr Val Gly Met Gln 100 105 110

Asn Cys Pro Lys Asp Gly Phe Pro Val Pro Ala Asn Ile Ile Trp His 115 120 125

Phe Lys Glu Asp Gly Thr Ile Phe His Pro His Ser Gly Leu Cys Leu 130 140

Ser Ala Tyr Arg Thr Pro Glu Gly Arg Pro Asp Val Gln Met Arg Thr 145 150 155 160 Cys Asp Ala Leu Asp Lys Asn Gln Ile Trp Ser Phe Glu Lys 165 170

<210>

<211> 168

<212> PRT

<213> Homo sapiens

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Asp Val Gly Asn Leu Thr Gln Gln Arg Glu Leu Arg Lys Lys Leu Lys
1 10 15

Cys Lys Ser Phe Lys Trp Tyr Leu Glu Asn Val Phe Pro Asp Leu Arg 20 25 30

Ala Pro Ile Val Arg Ala Ser Gly Val Leu Ile Asn Val Ala Leu Gly 35 40 45

Lys Cys Ile Ser Ile Glu Asn Thr Thr Val Ile Leu Glu Asp Cys Asp 50 60

Gly Ser Lys Glu Leu Gln Gln Phe Asn Tyr Thr Trp Leu Arg Leu Ile 65 70 75 80

Lys Cys Gly Glu Trp Cys Ile Ala Pro Ile Pro Asp Lys Gly Ala Val 85 90 95

Arg Leu His Pro Cys Asp Asn Arg Asn Lys Gly Leu Lys Trp Leu His 100

Lys Ser Thr Ser Val Phe His Pro Glu Leu Val Asn His Ile Val Phe

Glu Asn Asn Gln Gln Leu Leu Cys Leu Glu Gly Asn Phe Ser Gln Lys

Ile Leu Lys Val Ala Ala Cys Asp Pro Val Lys Pro Tyr Gln Lys Trp 145 150 155 160

Lys Phe Glu Lys Tyr Tyr Glu Ala 165

<210> 8

<211> 165

<212> PRT

<213> Homo sapiens

<400> 8

Ser Phe Gly Asp Ile Ser Glu Arg Leu Gln Leu Arg Glu Gln Leu His

Cys His Asn Phe Ser Trp Tyr Leu His Asn Val Tyr Pro Glu Met Phe 20 25 30

Val Pro Asp Leu Thr Pro Thr Phe Tyr Gly Ala Ile Lys Asn Leu Gly 35 40 45

Thr Asn Gln Cys Leu Asp Val Gly Glu Asn Asn Arg Gly Gly Lys Pro 50 60

Leu Ile Met Tyr Ser Cys His Gly Leu Gly Gly Asn Gln Tyr Phe Glu 65 70 75 80

Tyr Thr Thr Gln Arg Asp Leu Arg His Asn Ile Ala Lys Gln Leu Cys 85 90 95

Leu His Val Ser Lys Gly Ala Leu Gly Leu Gly Ser Cys His Phe Thr 100 105 110

Gly Lys Asn Ser Gln Val Pro Lys Asp Glu Glu Trp Glu Leu Ala Gln
115 120 125

Asp Gln Leu Ile Arg Asn Ser Gly Ser Gly Thr Cys Leu Thr Ser Gln 130 140

Asp Lys Lys Pro Ala Met Ala Pro Cys Asn Pro Ser Asp Pro His Gln 145 150 155 160

Leu Trp Leu Phe Val 165

<210>

<211> 166

<212>

<213> Homo sapiens

<400> 9

Tyr Gly Asp Ile Ser Glu Leu Lys Lys Phe Arg Glu Asp His Asn Cys 10 15

Gln Ser Phe Lys Trp Phe Met Glu Glu Ile Ala Tyr Asp Ile Thr Ser 20 25 30

His Tyr Pro Leu Pro Pro Lys Asn Val Asp Trp Gly Glu Ile Arg Gly 35 40 45

Phe Glu Thr Ala Tyr Cys Ile Asp Ser Met Gly Lys Thr Asn Gly Gly 50 55 60

Phe Val Glu Leu Gly Pro Cys His Arg Met Gly Gly Asn Gln Leu Phe 65 70 75 80

Arg Ile Asn Glu Ala Asn Gln Leu Met Gln Tyr Asp Gln Cys Leu Thr 85 90 95

Lys Gly Ala Asp Gly Ser Lys Val Met Ile Thr His Cys Asn Leu Asn 100 105 110

Glu Phe Lys Glu Trp Gln Tyr Phe Lys Asn Leu His Arg Phe Thr His 125

Ile Pro Ser Gly Lys Cys Leu Asp Arg Ser Glu Val Leu His Gln Val 130 135 140

Phe Ile Ser Asn Cys Asp Ser Ser Lys Thr Thr Gln Lys Trp Glu Met 145 150 155 160

Asn Asn Ile His Ser Val 165

<210> 10

<211> 179

<212> PRT

<213> Homo sapiens

<400> 10

Phe Gly Asp Val Ser Ser Arg Met Ala Leu Arg Glu Lys Leu Lys Cys $1 \hspace{1cm} 10 \hspace{1cm} 15$

Lys Thr Phe Asp Trp Tyr Leu Lys Asn Val Tyr Pro Leu Leu Lys Pro 20 25 30

Leu His Thr Ile Val Gly Tyr Gly Arg Met Lys Asn Leu Leu Asp Glu 35 40 45

Asn Val Cys Leu Asp Gln Gly Pro Val Pro Gly Asn Thr Pro Ile Met 50 55 60

Tyr Tyr Cys His Glu Phe Ser Ser Gln Asn Val Tyr Tyr His Leu Thr 65 70 75 80

Gly Glu Leu Tyr Val Gly Gln Leu Ile Ala Glu Ala Ser Ala Ser Asp 85 90 95

Arg Cys Leu Thr Asp Pro Gly Lys Ala Glu Lys Pro Thr Leu Glu Pro
100 105 110

Cys Ser Lys Ala Ala Lys Asn Arg Leu His Ile Tyr Trp Asp Phe Lys 115 120 125

Pro Gly Gly Ala Val Ile Asn Arg Asp Thr Lys Arg Cys Leu Glu Met 130 140

Lys Lys Asp Leu Leu Gly Ser His Val Leu Val Leu Gln Thr Cys Ser 145 150 155 160

Thr Gln Val Trp Glu Ile Gln His Thr Val Arg Asp Trp Gly Gln Thr 165 170 175

Asn Ser Gln

<210> 11

<211> 177

<212> PRT

<213> Homo sapiens

<400> 11

Phe Gly Asp Val Ser Glu Arg Leu Ala Leu Arg Gln Arg Leu Lys Cys
10 15

Arg Ser Phe Lys Trp Tyr Leu Glu Asn Val Tyr Pro Glu Met Arg Val 20 25 30

Tyr Asn Asn Thr Leu Thr Tyr Gly Glu Val Arg Asn Ser Lys Ala Ser 35 40 45

Ala Tyr Cys Leu Asp Gln Gly Ala Glu Asp Gly Asp Arg Ala Ile Leu 50 60

Tyr Pro Cys His Gly Met Ser Ser Gln Leu Val Arg Tyr Ser Ala Asp 65 70 75 80

Gly Leu Leu Gln Leu Gly Pro Leu Gly Ser Thr Ala Phe Leu Pro Asp 85 90 95

Ser Lys Cys Leu Val Asp Asp Gly Thr Gly Arg Met Pro Thr Leu Lys $100 \hspace{1cm} 105 \hspace{1cm} 110$

Arg Cys Glu Asp Val Ala Arg Pro Thr Gln Arg Leu Trp Asp Phe Thr 115 120 125

Gln Ser Gly Pro Ile Val Ser Arg Ala Thr Gly Arg Cys Leu Glu Val 130 135 140 Glu Met Ser Lys Asp Ala Asn Phe Gly Leu Arg Leu Val Val Gln Arg 145 150 155 160

Cys Ser Gly Gln Lys Trp Met Ile Arg Asn Trp Ile Lys His Ala Arg 165 170 175

His

<210>

12 187 <211> <212>

PRT <213> Homo sapiens

<400>

Ala Gly Asp Val Ala Val Gln Lys Lys Leu Arg Ser Ser Leu Asn Cys
1 10 15

Lys Ser Phe Lys Trp Phe Met Thr Lys Ile Ala Trp Asp Leu Pro Lys
20 25 30

Phe Tyr Pro Pro Val Glu Pro Pro Ala Ala Ala Trp Gly Glu Ile Arg 35 40 45

Asn Val Gly Thr Gly Leu Cys Ala Asp Thr Lys His Gly Ala Leu Gly 50 60

Ser Pro Leu Arg Leu Glu Gly Cys Val Arg Gly Arg Gly Glu Ala Ala 65 70 75 80

Trp Asn Asn Met Gln Val Phe Thr Phe Thr Trp Arg Glu Asp Ile Arg 85 90 95

Pro Gly Asp Pro Gln His Thr Lys Lys Phe Cys Phe Asp Ala Ile Ser 100 105 110

His Thr Ser Pro Val Thr Leu Tyr Asp Cys His Ser Met Lys Gly Asn 115 120 125

Gln Leu Trp Lys Tyr Arg Lys Asp Lys Thr Leu Tyr His Pro Val Ser 130 135 140

Gly Ser Cys Met Asp Cys Ser Glu Ser Asp His Arg Ile Phe Met Asn 145 150 155 160

Thr Cys Asn Pro Ser Ser Leu Thr Gln Gln Trp Leu Phe Glu His Thr

Asn Ser Thr Val Leu Glu Lys Phe Asn Arg Asn

180 185

<210> 13

<211> 181

<212> PRT

<213> Homo sapiens

<400> 13

Asn Ile Ser Glu Arg Val Glu Leu Arg Lys Leu Gly Cys Lys Ser 1 10 15

Phe Lys Trp Tyr Leu Asp Asn Val Tyr Pro Glu Met Gln Ile Ser Gly 20 25 30

Ser His Ala Lys Pro Gln Gln Pro Ile Phe Val Asn Arg Gly Pro Lys 35 40 45

Pro Lys Val Leu Gln Arg Gly Arg Leu Tyr His Leu Gln Thr Asn 50 60

Lys Cys Leu Val Ala Gln Gly Arg Pro Ser Gln Lys Gly Gly Leu Val 65 70 75 80

Val Leu Lys Ala Cys Asp Tyr Ser Asp Pro Asn Gln Ile Trp Ile Tyr 85 90 95

Asn Glu Glu His Glu Leu Val Leu Asn Ser Leu Leu Cys Leu Asp Met 100

Ser Glu Thr Arg Ser Ser Asp Pro Pro Arg Leu Met Lys Cys His Gly 115 120 115

Ser Gly Gly Ser Gln Gln Trp Thr Phe Gly Lys Asn Asn Arg Leu Tyr 130 140

Gln Val Ser Val Gly Gln Cys Leu Arg Ala Val Asp Pro Leu Gly Gln 145 150 155 160

Lys Gly Ser Val Ala Met Ala Ile Cys Asp Gly Ser Ser Ser Gln Gln 165 170 175

Trp His Leu Glu Gly 180

<210>

14 173 <211>

<212> PRT

<213> Homo sapiens

<400> 14 Asp Val Thr Glu Arg Lys Gln Leu Arg Asp Lys Leu Gln Cys Lys Asp
1 10 15

Phe Lys Trp Phe Leu Glu Thr Val Tyr Pro Glu Leu His Val Pro Glu 20 25 30

Asp Arg Pro Gly Phe Phe Gly Met Leu Gln Asn Lys Gly Leu Thr Asp 35 40 45

Tyr Cys Phe Asp Tyr Asn Pro Pro Asp Glu Asn Gln Ile Val Gly His 50 60

Gln Val Ile Leu Tyr Leu Cys His Gly Met Gly Gln Asn Gln Phe Phe 65 70 75 80

Glu Tyr Thr Ser Gln Lys Glu Ile Arg Tyr Asn Thr His Gln Pro Glu 85 90 95

Gly Cys Ile Ala Val Glu Ala Gly Met Asp Thr Leu Ile Met His Leu 100 105 110

Cys Glu Glu Thr Ala Pro Glu Asn Gln Lys Phe Ile Leu Gln Glu Asp

Gly Ser Leu Phe His Glu Gln Ser Lys Lys Cys Val Gln Ala Ala Arg 130 135 140

Lys Glu Ser Ser Asp Ser Phe Val Pro Leu Leu Arg Asp Cys Thr Asn 145 150 155 160

Ser Asp His Gln Lys Trp Phe Phe Lys Glu Arg Met Leu 165 170

<400> 15

Glu Lys Pro Asp Cys Met Glu Arg Leu Gln Leu Gln Arg Arg Leu Gly
10 15

Cys Arg Thr Phe His Trp Phe Leu Ala Asn Val Tyr Pro Glu Leu Tyr 20 25 30

Pro Ser Glu Pro Arg Pro Ser Phe Ser Gly Lys Leu His Asn Thr Gly 35 40 45

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<211>

<212> **PRT**

<213> Homo sapiens

Leu Gly Leu Cys Ala Asp Cys Gln Ala Glu Gly Asp Ile Leu Gly Cys 50 60

Pro Met Val Leu Ala Pro Cys Ser Asp Ser Arg Gln Gln Gln Tyr Leu 65 70 75 80

Gln His Thr Ser Arg Lys Glu Ile His Phe Gly Ser Pro Gln His Leu 85 90 95

Cys Phe Ala Val Arg Gln Glu Gln Val Ile Leu Gln Asn Cys Thr Glu 105

Glu Gly Leu Ala Ile His Gln Gln His Trp Asp Phe Gln Glu Asn Gly 115 120 125

Met Ile Val His Ile Leu Ser Gly Lys Cys Met Glu Ala Val Val Gln 130 135 140

Glu Asn Asn Lys Asp Leu Tyr Leu Arg Pro Cys Asp Gly Lys Ala Arg 145 150 155 160

Gln Gln Trp Arg Phe Asp Gln Ile Asn Ala Val Asp Glu Arg 165 170

16

<210> <211> 165

<212> PRT

<213> Homo sapiens

<400> 16

Tyr Gly Asp Val Ser Val Arg Lys Thr Leu Arg Glu Asn Leu Lys Cys $1 \hspace{1cm} 10 \hspace{1cm} 15$

Lys Pro Phe Ser Trp Tyr Leu Glu Asn Ile Tyr Pro Asp Ser Gln Ile 20 25 30

Pro Arg Arg Tyr Tyr Ser Leu Gly Glu Ile Arg Asn Val Glu Thr Asn 35 40 45

Gln Cys Leu Asp Asn Met Gly Arg Lys Glu Asn Glu Lys Val Gly Ile 50 60

Phe Asn Cys His Gly Met Gly Gly Asn Gln Val Phe Ser Tyr Thr Ala 65 70 75 80

Asp Lys Glu Ile Arg Thr Asp Asp Leu Cys Leu Asp Val Ser Arg Leu 85 90 95

Asn Gly Pro Val Ile Met Leu Lys Cys His His Met Arg Gly Asn Gln

100 105 110

Leu Trp Glu Tyr Asp Ala Glu Arg Leu Thr Leu Arg His Val Asn Ser 115 120 125

Asn Gln Cys Leu Asp Glu Pro Ser Glu Glu Asp Lys Met Val Pro Thr 130 135 140

Met Gln Asp Cys Ser Gly Ser Arg Ser Gln Gln Trp Leu Leu Arg Asn 145 150 155 160

Met Thr Leu Gly Thr 165

<210> 17

<211> 171

<212> PRT

<213> Homo sapiens

<400> 17

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Phe Gly Asn Val Glu Ser Arg Leu Asp Leu Arg Lys Asn Leu Arg Cys 10 15

Gln Ser Phe Lys Trp Tyr Leu Glu Asn Ile Tyr Pro Glu Leu Ser Ile 20 25 30

Pro Lys Glu Ser Ser Ile Gln Lys Gly Asn Ile Arg Gln Arg Gln Lys 35 40 45

Cys Leu Glu Ser Gln Arg Gln Asn Asn Gln Glu Thr Pro Asn Leu Lys 50 60

Leu Ser Pro Cys Ala Lys Val Lys Gly Glu Asp Ala Lys Ser Gln Val 65 70 75 80

Trp Ala Phe Thr Tyr Thr Gln Lys Ile Leu Gln Glu Glu Leu Cys Leu 85 90 95

Ser Val Ile Thr Leu Phe Pro Gly Ala Pro Val Val Leu Val Leu Cys 100 105 110

Lys Asn Gly Asp Asp Arg Gln Gln Trp Thr Lys Thr Gly Ser His Ile 115 120 125

Glu His Ile Ala Ser His Leu Cys Leu Asp Thr Asp Met Phe Gly Asp 130 135 140

Gly Thr Glu Asn Gly Lys Glu Ile Gly Val Asn Pro Cys Glu Ser Ser 145 150 155 160 Leu Met Ser Gln His Trp Asp Met Val Ser Ser 165 170

<210> 18

<211> 163 <212> PRT

<213> Homo sapiens

<400> 18

Ser Val Ala Thr Arg Ile Glu Gln Arg Lys Lys Met Asn Cys Lys Ser $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Phe Arg Trp Tyr Leu Glu Asn Val Tyr Pro Glu Leu Thr Val Pro Val 20 25 30

Lys Glu Ala Leu Pro Gly Ile Ile Lys Gln Gly Val Asn Cys Leu Glu 35 40 45

Ser Gln Gly Gln Asn Thr Ala Gly Asp Phe Leu Leu Gly Met Gly Ile $50 \hspace{1cm} 55 \hspace{1cm} 60$

Cys Arg Gly Ser Ala Lys Asn Pro Gln Pro Ala Gln Ala Trp Leu Phe 65 70 75 80

Ser Asp His Leu Ile Gln Gln Gln Gly Lys Cys Leu Ala Ala Thr Ser 85 90 95

Thr Leu Met Ser Ser Pro Gly Ser Pro Val Ile Leu Gln Met Cys Asn $100 \hspace{1cm} 105 \hspace{1cm} 110$

Pro Arg Glu Gly Lys Gln Lys Trp Arg Arg Lys Gly Ser Phe Ile Gln 115 120 125

His Ser Val Ser Gly Leu Cys Leu Glu Thr Lys Pro Ala Gln Leu Val 130 135 140

Thr Ser Lys Cys Gln Ala Asp Ala Gln Ala Gln Gln Trp Gln Leu Leu 145 150 155 160

Pro His Thr

<210> 19

<211> 8

<212> PRT <213> Homo sapiens

<400> 19

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<220> <223>	PCR primer	
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tggtgccg	gcg	cggcagccat	atggctagca	tgactggtgg	acagcaaatg	ggtcgcggaa	120
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	53 cgg	ccgcagcagc	catcatcatc	atcatcacag	cagcggcctg	gtgccgcgcg	60
gcagccat	tat	ggctagcatg	actggtggac	agcaaatgga	tccactagtt	ctagagcggc	120
cgc							123
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ctgttggt	tgc	tcctggcgct	actggcgttg	gccgggctgg	gctcggtgct	gcgggcgcag	120
cgtgggg	ccg	gggccggggc	tgccgagccg	ggacccccgc	gcaccccgcg	ccccgggcgg	180
cgcgagco	cgg	tcatgccgcg	gccgccggtg	ccggcgaacg	cgctgggcgc	gcggggcgag	240
gcggtgcg	ggc	tgcagctgca	gggcgaggag	ctgcggctgc	aggaggagag	cgtgcggctg	300
caccagat	tta	acatctacct	cagcgaccgc	atctcactgc	accgccgcct	gcccgagcgc	360
tggaacco	cgc	tgtgcaaaga	gaagaaatat	gattatgata	atttgcccag	gacatctgtt	420
atcatago	cat	tttataatga	agcctggtca	actctccttc	ggacagttta	cagtgtcctt	480
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Leu Gly Ser Val Leu Arg Ala Gln Arg Gly Ala Gly Ala Gly Ala Ala 35 40 45

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Met Pro Arg Pro Pro Val Pro Ala Asn Ala Leu Gly Ala Arg Gly Glu 65 70 75 80 22

⁵⁵ 581 <211>

<212> PRT

<213> Homo sapiens

<400> 55

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Gly Glu Asn Leu Glu Phe Ser Phe Arg Ile Trp Gln Cys Gly Gly Val 340 345 350 Leu Glu Thr His Pro Cys Ser His Val Gly His Phe Ser Pro Ser Lys 355 360 365 Leu Pro Thr Pro Arg Asn Lys Ala Leu Ala Asn Ser Val Arg Ala Ala 370 380 Glu Val Trp Met Asp Glu Phe Lys Glu Leu Tyr Tyr His Arg Asn Pro 385 390 395 400 Arg Ala Arg Leu Glu Pro Phe Gly Asp Val Thr Glu Arg Lys Gln Leu Arg Asp Lys Leu Gln Cys Lys Asp Phe Lys Trp Phe Leu Glu Thr Val Tyr Pro Glu Leu His Val Pro Glu Asp Arg Pro Gly Phe Phe Gly Met Leu Gln Asn Lys Gly Leu Thr Asp Tyr Cys Phe Asp Tyr Asn Pro Pro Asp Glu Asn Gln Ile Val Gly His Gln Val Ile Leu Tyr Leu Cys His 465 470 475 480 Gly Met Gly Gln Asn Gln Phe Phe Glu Tyr Thr Ser Gln Lys Glu Ile Arg Tyr Asn Thr His Gln Pro Glu Gly Cys Ile Ala Val Glu Ala Gly 500 505 510 Met Asp Thr Leu Ile Met His Leu Cys Glu Glu Thr Ala Pro Glu Asn Gln Lys Phe Ile Leu Gln Glu Asp Gly Ser Leu Phe His Glu Gln Ser 530 540 Lys Lys Cys Val Gln Ala Ala Arg Lys Glu Ser Ser Asp Ser Phe Val 545 550 555 560 Pro Leu Leu Arg Asp Cys Thr Asn Ser Asp His Gln Lys Trp Phe Phe 565 570 575 Lys Glu Arg Met Leu 580

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<211> 639

<212> PRT

<213> Homo sapiens

<400> 57

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Leu His Pro Pro His His Thr Leu His Gln Thr Val Thr Ala Gln Ala 35 40 45

Ser Lys His Ser Pro Glu Ala Arg Tyr Arg Leu Asp Phe Gly Glu Ser 50 60

Gln Asp Trp Val Leu Glu Ala Glu Asp Glu Gly Glu Glu Tyr Ser Pro 65 70 75 80

Leu Glu Gly Leu Pro Pro Phe Ile Ser Leu Arg Glu Asp Gln Leu Leu 85 90 95

Val Ala Val Ala Leu Pro Gln Ala Arg Arg Asn Gln Ser Gln Gly Arg 100 105 110

Arg Gly Gly Ser Tyr Arg Leu Ile Lys Gln Pro Arg Arg Gln Asp Lys 115 120 125

Glu Ala Pro Lys Arg Asp Trp Gly Ala Asp Glu Asp Gly Glu Val Ser 130 135 140

Glu Glu Glu Leu Thr Pro Phe Ser Leu Asp Pro Arg Gly Leu Gln 145 150 155 160

Glu Ala Leu Ser Ala Arg Ile Pro Leu Gln Arg Ala Leu Pro Glu Val 165 170 175

Arg His Pro Leu Cys Leu Gln Gln His Pro Gln Asp Ser Leu Pro Thr 180 185 190 Ala Ser Val Ile Leu Cys Phe His Asp Glu Ala Trp Ser Thr Leu Leu 195 200 205 Thr Val His Ser Ile Leu Asp Thr Val Pro Arg Ala Phe Leu Lys 210 220 Glu Ile Ile Leu Val Asp Asp Leu Ser Gln Gln Gly Gln Leu Lys Ser 225 230 235 240 Ala Leu Ser Glu Tyr Val Ala Arg Leu Glu Gly Val Lys Leu Leu Arg 245 250 255 Ser Asn Lys Arg Leu Gly Ala Ile Arg Ala Arg Met Leu Gly Ala Thr 260 265 270 Arg Ala Thr Gly Asp Val Leu Val Phe Met Asp Ala His Cys Glu Cys Pro Gly Trp Leu Glu Pro Leu Leu Ser Arg Ile Ala Gly Asp Arg Ser Arg Val Val Ser Pro Val Ile Asp Val Ile Asp Trp Lys Thr Phe 305 310 315 Gln Tyr Tyr Pro Ser Lys Asp Leu Gln Arg Gly Val Leu Asp Trp Lys 325 330 335 Leu Asp Phe His Trp Glu Pro Leu Pro Glu His Val Arg Lys Ala Leu 340 345 350 Gln Ser Pro Ile Ser Pro Ile Arg Ser Pro Val Val Pro Gly Glu Val 355 360 365 Val Ala Met Asp Arg His Tyr Phe Gln Asn Thr Gly Ala Tyr Asp Ser 370 380 Leu Met Ser Leu Arg Gly Gly Glu Asn Leu Glu Leu Ser Phe Lys Ala 385 390 395 400 Trp Leu Cys Gly Gly Ser Val Glu Ile Leu Pro Cys Ser Arg Val Gly
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435 440 445

Lys	G1u 450	Thr	Phe	Tyr	Lys	ніs 455	Ser	Pro	Glu	Ala	Phe 460	Ser	Leu	Ser	Lys
Ala 465	Glu	Lys	Pro	Asp	Cys 470	Met	Glu	Arg	Leu	Gln 475	Leu	Gln	Arg	Arg	Leu 480
Gly	Cys	Arg	Thr	Phe 485	His	Trp	Phe	Leu	Ala 490	Asn	٧a٦	Tyr	Pro	Glu 495	Leu
Tyr	Pro	Ser	Glu 500	Pro	Arg	Pro	Ser	Phe 505	Ser	Gly	Lys	Leu	ніs 510	Asn	Thr
Gly	Leu	Gly 515	Leu	Cys	Ala	Asp	Cys 520	Gln	Ala	Glu	Gly	Asp 525	Ile	Leu	Gly
Cys	Pro 530	Met	٧a٦	Leu	Ala	Pro 535	Cys	Ser	Asp	Ser	Arg 540	Gln	Gln	Gln	Tyr
Leu 545	Gln	His	Thr	Ser	Arg 550	Lys	Glu	Ile	His	Phe 555	Gly	Ser	Pro	Gln	ніs 560
Leu	Cys	Phe	Ala	va1 565	Arg	Gln	Glu	Gln	Va1 570	Ile	Leu	Gln	Asn	Cys 575	Thr
Glu	Glu	Gly	L eu 580	Ala	Ile	His	Gln	G]n 585	His	Тгр	Asp	Phe	Gln 590	Glu	Asn
Gly	Met	Ile 595	۷a٦	His	Ile	Leu	ser 600	Gly	Lys	Cys	Met	G]u 605	Ala	val	val
Gln	Glu 610	Asn	Asn	Lys	Asp	Leu 615	Tyr	Leu	Arg	Pro	Cys 620	Asp	Gly	Lys	Ala
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<212> DNA

<213> Homo sapiens

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Lys Cys Asp Asp Lys Lys Glu Arg Ser Leu Leu Pro Ala Leu Arg Ala 35 40 45

PRT Homo sapiens

<400> 59

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65 70 75 80 Asn Gln Phe Asn Leu Met Ala Ser Asp Leu Ile Ala Leu Asn Arg Ser 85 90 95 Leu Pro Asp Val Arg Leu Glu Gly Cys Lys Thr Lys Val Tyr Pro Asp 100 105 110 Glu Leu Pro Asn Thr Ser Val Val Ile Val Phe His Asn Glu Ala Trp 115 120 125 Ser Thr Leu Leu Arg Thr Val Tyr Ser Val Ile Asn Arg Ser Pro His Tyr Leu Leu Ser Glu Val Ile Leu Val Asp Asp Ala Ser Glu Arg Asp 145 150 155 160 Phe Leu Lys Leu Thr Leu Glu Asn Tyr Val Lys Asn Leu Glu Val Pro 165 170 175 Val Lys Ile Ile Arg Met Glu Glu Arg Ser Gly Leu Ile Arg Ala Arg 180 185 190 Leu Arg Gly Ala Ala Ala Ser Lys Gly Gln Val Ile Thr Phe Leu Asp 195 200 205 Ala His Cys Glu Cys Thr Leu Gly Trp Leu Glu Pro Leu Leu Ala Arg 210 215 220 Ile Lys Glu Asp Arg Lys Thr Val Val Cys Pro Ile Ile Asp Val Ile 225 230 235 240 Ser Asp Asp Thr Phe Glu Tyr Met Ala Gly Ser Asp Met Thr Tyr Gly 245 250 255 Gly Phe Asn Trp Lys Leu Asn Phe Arg Trp Tyr Pro Val Pro Gln Arg 260 265 270 Glu Met Asp Arg Arg Lys Gly Asp Arg Thr Leu Pro Val Arg Thr Pro 275 280 285 Thr Met Ala Gly Gly Leu Phe Ser Ile Asp Arg Asn Tyr Phe Glu Glu 300 30

Ile Gly Thr Tyr Asp Ala Gly Met Asp Ile Trp Gly Glu Asn Leu 305 310 315 320 Glu Met Ser Phe Arg Ile Trp Gln Cys Gly Gly Ser Leu Glu Ile Val 325 330 335 Thr Cys Ser His Val Gly His Val Phe Arg Lys Ala Thr Pro Tyr Thr 340 345 350 Phe Pro Gly Gly Thr Gly His Val Ile Asn Lys Asn Asn Arg Arg Leu 355 360 365 Ala Glu Val Trp Met Asp Glu Phe Lys Asp Phe Phe Tyr Ile Ile Ser 370 375 380 Pro Gly Val Val Lys Val Asp Tyr Gly Asp Val Ser Val Arg Lys Thr Leu Arg Glu Asn Leu Lys Cys Lys Pro Phe Ser Trp Tyr Leu Glu Asn Ile Tyr Pro Asp Ser Gln Ile Pro Arg Arg Tyr Tyr Ser Leu Gly Glu 420 430 Ile Arg Asn Val Glu Thr Asn Gln Cys Leu Asp Asn Met Gly Arg Lys 435 Glu Asn Glu Lys Val Gly Ile Phe Asn Cys His Gly Met Gly Gly Asn 450 460 Gln Val Phe Ser Tyr Thr Ala Asp Lys Glu Ile Arg Thr Asp Asp Leu 465 470 475 480 470 465 Cys Leu Asp Val Ser Arg Leu Asn Gly Pro Val Ile Met Leu Lys Cys 485 490 495 His His Met Arg Gly Asn Gln Leu Trp Glu Tyr Asp Ala Glu Arg Leu 500 505 510 Thr Leu Arg His Val Asn Ser Asn Gln Cys Leu Asp Glu Pro Ser Glu 515 520 525 Glu Asp Lys Met Val Pro Thr Met Gln Asp Cys Ser Gly Ser Arg Ser 530 540 Gln Gln Trp Leu Leu Arg Asn Met Thr Leu Gly Thr 545 550 555

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<211> 552 <212> PRT

<213> Homo sapiens

<400> 61

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Val Pro Thr Gly Pro Glu Val Gln Thr Pro Lys Pro Ser Asp Ala Asp 35 40 45

Trp Asp Asp Leu Trp Asp Gln Phe Asp Glu Arg Arg Tyr Leu Asn Ala 50 60

Lys Lys Trp Arg Val Gly Asp Asp Pro Tyr Lys Leu Tyr Ala Phe Asn 65 70 75 80

Gln Arg Glu Ser Glu Arg Ile Ser Ser Asn Arg Ala Ile Pro Asp Thr 85 90 95

Arg His Leu Arg Cys Thr Leu Leu Val Tyr Cys Thr Asp Leu Pro Pro $100 \hspace{1cm} 105 \hspace{1cm} 110$

Thr Ser Ile Ile Ile Thr Phe His Asn Glu Ala Arg Ser Thr Leu Leu 115 120 125

Arg Thr Ile Arg Ser Val Leu Asn Arg Thr Pro Thr His Leu Ile Arg 130 135 140

Glu Ile Ile Leu Val Asp Asp Phe Ser Asn Asp Pro Asp Asp Cys Lys 155 150 155

Gln Leu Ile Lys Leu Pro Lys Val Lys Cys Leu Arg Asn Asn Glu Arg 165 170 175

Gln Gly Leu Val Arg Ser Arg Ile Arg Gly Ala Asp Ile Ala Gln Gly 180 185 190

Thr Thr Leu Thr Phe Leu Asp Ser His Cys Glu Val Asn Arg Asp Trp Leu Gln Pro Leu Leu His Arg Val Lys Glu Asp Tyr Thr Arg Val Val 210 220 Cys Pro Val Ile Asp Ile Ile Asn Leu Asp Thr Phe Thr Tyr Ile Glu 225 230 235 240 Ser Ala Ser Glu Leu Arg Gly Gly Phe Asp Trp Ser Leu His Phe Gln 245 250 255 Trp Glu Gln Leu Ser Pro Glu Gln Lys Leu Gly Ala Trp Thr Pro Arg 260 265 270 Lys Pro Ile Arg Thr Pro Ile Ile Ala Gly Gly Leu Phe Val Ile Asp 275 280 285 Ala Trp Phe Asp Tyr Leu Gly Lys Tyr Asp Met Asp Met Asp Ile 290 295 300 Trp Gly Gly Glu Asn Phe Glu Ile Ser Phe Arg Val Trp Met Cys Gly 315 310 320 Gly Ser Leu Glu Ile Val Pro Cys Ser Arg Val Gly His Val Phe Arg 325 330 335 Lys Lys His Pro Tyr Val Phe Pro Asp Gly Asn Ala Asn Thr Tyr Ile 340 345 350 Lys Asn Thr Lys Arg Thr Ala Glu Val Trp Met Asp Glu Tyr Lys Gln Tyr Tyr Tyr Ala Ala Arg Pro Phe Ala Leu Glu Arg Pro Phe Gly Asn 370 380 Val Glu Ser Arg Leu Asp Leu Arg Lys Asn Leu Arg Cys Gln Ser Phe 385 390 395 400 Lys Trp Tyr Leu Glu Asn Ile Tyr Pro Glu Leu Ser Ile Pro Lys Glu
405 410 415 Ser Ser Ile Gln Lys Gly Asn Ile Arg Gln Arg Gln Lys Cys Leu Glu 420 425 430 Ser Gln Arg Gln Asn Asn Gln Glu Thr Pro Asn Leu Lys Leu Ser Pro 435 440 445

Cys Ala Lys Val Lys Gly Glu Asp Ala Lys Ser Gln Val Trp Ala Phe 450 455 460

Thr Tyr Thr Gln Gln Ile Leu Gln Glu Glu Leu Cys Leu Ser Val Ile 465 470 475 480

Thr Leu Phe Pro Gly Ala Pro Val Val Leu Val Leu Cys Lys Asn Gly 485 490 495

Asp Asp Arg Gln Gln Trp Thr Lys Thr Gly Ser His Ile Glu His Ile 500 505 510

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Gln Leu Arg Glu Asp Arg Thr Ile Pro Leu Ile Val Thr Gly Thr Pro 50 60

Ser Lys Gly Phe Asp Glu Lys Ala Tyr Leu Ser Ala Lys Gln Leu Lys 65 70 75 80

Ala Gly Glu Asp Pro Tyr Arg Gln His Ala Phe Asn Gln Leu Glu Ser 85 90 95

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PRT

<213> Homo sapiens

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Ala Arg Pro Ser Ala Ile Gly Lys Ala Phe Gly Ser Val Ala Thr Arg 385 390 395 400

Ile Glu Gln Arg Lys Lys Met Asn Cys Lys Ser Phe Arg Trp Tyr Leu 405 410 415

Glu Asn Val Tyr Pro Glu Leu Thr Val Pro Val Lys Glu Ala Leu Pro 420 425 430

Gly Ile Ile Lys Gln Gly Val Asn Cys Leu Glu Ser Gln Gly Gln Asn 435 440 445

Thr Ala Gly Asp Phe Leu Leu Gly Met Gly Ile Cys Arg Gly Ser Ala 450 460

Lys Asn Pro Gln Pro Ala Gln Ala Trp Leu Phe Ser Asp His Leu Ile 465 470 475 480

Gln Gln Gln Gly Lys Cys Leu Ala Ala Thr Ser Thr Leu Met Ser Ser 485 490 495

Pro Gly Ser Pro Val Ile Leu Gln Met Cys Asn Pro Arg Glu Gly Lys 500 505 510

Gln Lys Trp Arg Arg Lys Gly Ser Phe Ile Gln His Ser Val Ser Gly 515 520 525

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tatacto	gcca acaaagaaat tagaacagat gacctttgct tggatgtttc caaacttaat	300
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ccagtgaaat taaccctgca gcatgtgaac agtaatcagt gcctggataa agccacagaa 420 480 gaggatagcc aggtgcccag cattagagac tgcaatggaa gtcggtccca gcagtggctt 513 cttcgaaacg tcacccttcc agaaatattc tga

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<213> Homo sapiens

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Pro Arg His Tyr Phe Ser Leu Gly Glu Ile Arg Asn Val Glu Thr Asn 35 40 45

Gln Cys Leu Asp Asn Met Ala Arg Lys Glu Asn Glu Lys Val Gly Ile 50 60

Phe Asn Cys His Gly Met Gly Gly Asn Gln Val Phe Ser Tyr Thr Ala 65 70 75 80

Asn Lys Glu Ile Arg Thr Asp Asp Leu Cys Leu Asp Val Ser Lys Leu 85 90 95

Asn Gly Pro Val Thr Met Leu Lys Cys His His Leu Lys Gly Asn Gln
100 105 110

Leu Trp Glu Tyr Asp Pro Val Lys Leu Thr Leu Gln His Val Asn Ser 115 120 125

Asn G]n Cys Leu Asp Lys Ala Thr Glu Glu Asp Ser Gln Val Pro Ser

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360	aagcgtggag	gcgggggcct	acggccaaga	ggacagtcgc	acctgtgcct	gtgggcagca
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Leu Gln Gln Gly Thr Asn Cys Leu Asp Thr Leu Gly His Phe Ala Asp 20 25 30

Gly Val Val Gly Val Tyr Glu Cys His Asn Ala Gly Gly Asn Gln Glu 35 40 45

Trp Ala Leu Thr Lys Glu Lys Ser Val Lys His Met Asp Leu Cys Leu 50 60

Thr Val Val Asp Arg Ala Pro Gly Ser Leu Ile Lys Leu Gln Gly Cys 65 70 75 80

Arg Glu Asn Asp Ser Arg Gln Lys Trp Glu Gln Ile Glu Gly Asn Ser 85 90 95

Lys Leu Arg His Val Gly Ser Asn Leu Cys Leu Asp Ser Arg Thr Ala 100 105 110

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Pro Asp Leu Asn Pro Val Ile Ser Gly Tyr Ile Lys Ser Val Gly Gln 35 40 45

Pro Leu Cys Leu Asp Val Gly Glu Asn Asn Gln Gly Gly Lys Pro Leu 50 60

Ile Met Tyr Thr Cys His Gly Leu Gly Gly Asn Gln Tyr Phe Glu Tyr 65 70 75 80

Ser Ala Gln His Glu Ile Arg His Asn Ile Gln Lys Glu Leu Cys Leu 85 90 95

His Ala Ala Gln Gly Leu Val Gln Leu Lys Ala Cys Thr Tyr Lys Gly
100 105 110

His Lys Thr Val Val Thr Gly Glu Gln Ile Trp Glu Ile Gln Lys Asp 115 120 125

Gln Leu Leu Tyr Asn Pro Phe Leu Lys Met Cys Leu Ser Ala Asn Gly

Glu His Pro Ser Leu Val Ser Cys Asn Pro Ser Asp Pro Leu Gln Lys 145 150 155 160

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Ile Ser Ser Glu Cys Leu Asp Tyr Asn Ser Pro Asp Asn Asn Pro Thr 50 60
Gly Ala Asn Leu Ser Leu Phe Gly Cys His Gly Gln Gly Gly Asn Gln 65 75 80
Phe Phe Glu Tyr Thr Ser Asn Lys Glu Ile Arg Phe Asn Ser Val Thr 85 90 95
Glu Leu Cys Ala Glu Val Pro Glu Gln Lys Asn Tyr Val Gly Met Gln 100 105 110

Asn Cys Pro Lys Asp Gly Phe Pro Val Pro Ala Asn Ile Ile Trp His 115 120 125

Phe Lys Glu Asp Gly Thr Ile Phe His Pro His Ser Gly Leu Cys Leu 130 140

Ser Ala Tyr Arg Thr Pro Glu Gly Arg Pro Asp Val Gln Met Arg Thr 145 150 155 160

Cys Asp Ala Leu Asp Lys Asn Gln Ile Trp Ser Phe Glu Lys 165 170

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Cys Lys Ser Phe Lys Trp Tyr Leu Glu Asn Val Phe Pro Asp Leu Arg 20 25 30

Ala Pro Ile Val Arg Ala Ser Gly Val Leu Ile Asn Val Ala Leu Gly $40 \hspace{1cm} 45$

Lys Cys Ile Ser Ile Glu Asn Thr Thr Val Ile Leu Glu Asp Cys Asp 50 55 60

Gly Ser Lys Glu Leu Gln Gln Phe Asn Tyr Thr Trp Leu Arg Leu Ile 65 70 75 80 Lys Cys Gly Glu Trp Cys Ile Ala Pro Ile Pro Asp Lys Gly Ala Val 85 90 95 Arg Leu His Pro Cys Asp Asn Arg Asn Lys Gly Leu Lys Trp Leu His
100 105 110 Lys Ser Thr Ser Val Phe His Pro Glu Leu Val Asn His Ile Val Phe Glu Asn Asn Gln Gln Leu Leu Cys Leu Glu Gly Asn Phe Ser Gln Lys 130 135 140 Ile Leu Lys Val Ala Ala Cys Asp Pro Val Lys Pro Tyr Gln Lys Trp 145 150 155 160 Lys Phe Glu Lys Tyr Tyr Glu Ala 165 <210> 106 <211> 498 <212> DNA <213> Homo sapiens <400> 106 60 tccttcggtg acatttcgga acgactgcag ctgagggaac aactgcactg tcacaacttt 120 180 tatggtgcca tcaagaacct cggcaccaac caatgcctgg atgtgggtga gaacaaccgc ggggggaagc ccctcatcat gtactcctgc cacggccttg gcggcaacca gtactttgag 240 300 tacacaactc agagggacct tcgccacaac atcgcaaagc agctgtgtct acatgtcagc 360 aagggtgctc tgggccttgg gagctgtcac ttcactggca agaatagcca ggtccccaag gacgaggaat gggaattggc ccaggatcag ctcatcagga actcaggatc tggtacctgc 420 480 ctgacatccc aggacaaaaa gccagccatg gccccctgca atcccagtga cccccatcag 498 ttgtggctct ttgtctag <210> 107 165 <212> PRT <213> Homo sapiens <400> 107

Ser Phe Gly Asp Ile Ser Glu Arg Leu Gln Leu Arg Glu Gln Leu His 1 10 15

Cys His Asn Phe Ser Trp Tyr Leu His Asn Val Tyr Pro Glu Met Phe 20 25 30 Val Pro Asp Leu Thr Pro Thr Phe Tyr Gly Ala Ile Lys Asn Leu Gly 35 40 45 Thr Asn Gln Cys Leu Asp Val Gly Glu Asn Asn Arg Gly Gly Lys Pro 50 60 Leu Ile Met Tyr Ser Cys His Gly Leu Gly Gly Asn Gln Tyr Phe Glu 65 70 75 80 Tyr Thr Thr Gln Arg Asp Leu Arg His Asn Ile Ala Lys Gln Leu Cys 85 90 95 Leu His Val Ser Lys Gly Ala Leu Gly Leu Gly Ser Cys His Phe Thr 100 105 110 Gly Lys Asn Ser Gln Val Pro Lys Asp Glu Glu Trp Glu Leu Ala Gln 115 120 125 Gln Leu Ile Arg Asn Ser Gly Ser Gly Thr Cys Leu Thr Ser Gln 130 140 Asp Lys Lys Pro Ala Met Ala Pro Cys Asn Pro Ser Asp Pro His Gln 145 150 155 160 Leu Trp Leu Phe Val <210> 108 501 DNA Homo sapiens <400>

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His Tyr Pro Leu Pro Pro Lys Asn Val Asp Trp Gly Glu Ile Arg Gly 35 40 45

Phe Glu Thr Ala Tyr Cys Ile Asp Ser Met Gly Lys Thr Asn Gly Gly 50 55 60

Phe Val Glu Leu Gly Pro Cys His Arg Met Gly Gly Asn Gln Leu Phe 70 75 80

Arg Ile Asn Glu Ala Asn Gln Leu Met Gln Tyr Asp Gln Cys Leu Thr 85 90 95

Lys Gly Ala Asp Gly Ser Lys Val Met Ile Thr His Cys Asn Leu Asn $100 \hspace{1cm} 105 \hspace{1cm} 110$

Glu Phe Lys Glu Trp Gln Tyr Phe Lys Asn Leu His Arg Phe Thr His 115 120 125

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<400> 110

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atcatgtatt actgccatga attcagctca cagaatgtct actatcacct aactggggag 240 ctctatgtgg gacaactgat tgcagaggcc agtgctagtg atcgctgcct gacagaccct 300 ggcaaggcgg agaagcccac cttagaacca tgctccaagg cagctaagaa tagactgcat 360 atatattggg attttaaacc gggaggagct gtcataaaca gagataccaa gcggtgtctg 420 gagatgaaga aggatctttt gggtagccac gtgcttgtgc tccagacctg tagcacgcaa 480 gtgtgggaaa tccagcacac tgtcagagac tggggtcaga ccaacagcca gtga 534

<210> 111 <211> 179

<211> 179 <212> PRT

<213> Homo sapiens

<400> 111

Phe Gly Asp Val Ser Ser Arg Met Ala Leu Arg Glu Lys Leu Lys Cys
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Lys Thr Phe Asp Trp Tyr Leu Lys Asn Val Tyr Pro Leu Leu Lys Pro 20 25 30

Leu His Thr Ile Val Gly Tyr Gly Arg Met Lys Asn Leu Leu Asp Glu 35 40 45

Asn Val Cys Leu Asp Gln Gly Pro Val Pro Gly Asn Thr Pro Ile Met 50 55 60

Tyr Tyr Cys His Glu Phe Ser Ser Gln Asn Val Tyr Tyr His Leu Thr 65 70 75 80

Gly Glu Leu Tyr Val Gly Gln Leu Ile Ala Glu Ala Ser Ala Ser Asp 85 90 95

Arg Cys Leu Thr Asp Pro Gly Lys Ala Glu Lys Pro Thr Leu Glu Pro 100 105 110

Cys Ser Lys Ala Ala Lys Asn Arg Leu His Ile Tyr Trp Asp Phe Lys 115 120 125

Pro Gly Gly Ala Val Ile Asn Arg Asp Thr Lys Arg Cys Leu Glu Met 130 140

Lys Lys Asp Leu Leu Gly Ser His Val Leu Val Leu Gln Thr Cys Ser 145 150 155 160

Thr Gln Val Trp Glu Ile Gln His Thr Val Arg Asp Trp Gly Gln Thr 165 170 175 112

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Phe Gly Asp Val Ser Glu Arg Leu Ala Leu Arg Gln Arg Leu Lys Cys
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Arg Ser Phe Lys Trp Tyr Leu Glu Asn Val Tyr Pro Glu Met Arg Val 20 25 30
Tyr Asn Asn Thr Leu Thr Tyr Gly Glu Val Arg Asn Ser Lys Ala Ser 35 40 45
Ala Tyr Cys Leu Asp Gln Gly Ala Glu Asp Gly Asp Arg Ala Ile Leu 50 60
Tyr Pro Cys His Gly Met Ser Ser Gln Leu Val Arg Tyr Ser Ala Asp 65 70 75 80
Gly Leu Leu Gln Leu Gly Pro Leu Gly Ser Thr Ala Phe Leu Pro Asp 85 90 95
Ser Lys Cys Leu Val Asp Asp Gly Thr Gly Arg Met Pro Thr Leu Lys
100 105 110
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60

120 180

240

300

360

420

480

Arg Cys Glu Asp Val Ala Arg Pro Thr Gln Arg Leu Trp Asp Phe Thr 115 120 125

Gln Ser Gly Pro Ile Val Ser Arg Ala Thr Gly Arg Cys Leu Glu Val 130 135 140

Glu Met Ser Lys Asp Ala Asn Phe Gly Leu Arg Leu Val Val Gln Arg 145 150 155 160

Cys Ser Gly Gln Lys Trp Met Ile Arg Asn Trp Ile Lys His Ala Arg 165 170 175

His

<210> 114 <211> 564 <212> DNA

<213> Homo sapiens

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<210> 115

<211> 187

<212> PRT

<213> Homo sapiens

<400> 115

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Lys Ser Phe Lys Trp Phe Met Thr Lys Ile Ala Trp Asp Leu Pro Lys 20 25 30

Phe Tyr Pro Pro Val Glu Pro Pro Ala Ala Ala Trp Gly Glu Ile Arg 35 40 45 Asn Val Gly Thr Gly Leu Cys Ala Asp Thr Lys His Gly Ala Leu Gly 50 60

Ser Pro Leu Arg Leu Glu Gly Cys Val Arg Gly Arg Gly Glu Ala Ala 65 70 75 80

Trp Asn Asn Met Gln Val Phe Thr Phe Thr Trp Arg Glu Asp Ile Arg 85 90 95

Pro Gly Asp Pro Gln His Thr Lys Lys Phe Cys Phe Asp Ala Ile Ser 100 105 110

His Thr Ser Pro Val Thr Leu Tyr Asp Cys His Ser Met Lys Gly Asn 115 120 125

Gln Leu Trp Lys Tyr Arg Lys Asp Lys Thr Leu Tyr His Pro Val Ser 130 135 140

Gly Ser Cys Met Asp Cys Ser Glu Ser Asp His Arg Ile Phe Met Asn 150 155 160

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<210> 116

<211> 549

<212> DNA

<213> Homo sapiens

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<210> 117

<211> 181

<212> PRT

<213> Homo sapiens

<400> 117

Asn Ile Ser Glu Arg Val Glu Leu Arg Lys Lys Leu Gly Cys Lys Ser $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Phe Lys Trp Tyr Leu Asp Asn Val Tyr Pro Glu Met Gln Ile Ser Gly 20 25 30

Ser His Ala Lys Pro Gln Gln Pro Ile Phe Val Asn Arg Gly Pro Lys 35 40 45

Arg Pro Lys Val Leu Gln Arg Gly Arg Leu Tyr His Leu Gln Thr Asn 50 60

Lys Cys Leu Val Ala Gln Gly Arg Pro Ser Gln Lys Gly Gly Leu Val 65 70 75 80

Val Leu Lys Ala Cys Asp Tyr Ser Asp Pro Asn Gln Ile Trp Ile Tyr 85 90 95

Asn Glu Glu His Glu Leu Val Leu Asn Ser Leu Leu Cys Leu Asp Met 100 105 110

Ser Glu Thr Arg Ser Ser Asp Pro Pro Arg Leu Met Lys Cys His Gly 115 120 125

Ser Gly Gly Ser Gln Gln Trp Thr Phe Gly Lys Asn Asn Arg Leu Tyr 130 135 140

Gln Val Ser Val Gly Gln Cys Leu Arg Ala Val Asp Pro Leu Gly Gln 145 150 155 160

Lys Gly Ser Val Ala Met Ala Ile Cys Asp Gly Ser Ser Ser Gln Gln 165 170 175

Trp His Leu Glu Gly 180

<210> 118

<211> 525

<212> DNA

<213> Homo sapiens

<400> 118

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120 ttcttggaga ctgtgtatcc agaactgcat gtgcctgagg acaggcctgg cttcttcggg 180 atgctccaga acaaaggact aacagactac tgctttgact ataaccctcc cgatgaaaac 240 cagattgtgg gacaccaggt cattctgtac ctctgtcatg ggatgggcca gaatcagttt 300 ttcgagtaca cgtcccagaa agaaatacgc tataacaccc accagcctga gggctgcatt gctgtggaag caggaatgga tacccttatc atgcatctct gcgaagaaac tgccccagag 360 420 aatcagaagt tcatcttgca ggaggatgga tctttatttc acgaacagtc caagaaatgt 480 gtccaggctg cgaggaagga gtcgagtgac agtttcgttc cactcttacg agactgcacc 525 aactcggatc atcagaaatg gttcttcaaa gagcgcatgt tatga

<400> 119

Asp Val Thr Glu Arg Lys Gln Leu Arg Asp Lys Leu Gln Cys Lys Asp $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Phe Lys Trp Phe Leu Glu Thr Val Tyr Pro Glu Leu His Val Pro Glu 20 25 30

Asp Arg Pro Gly Phe Phe Gly Met Leu Gln Asn Lys Gly Leu Thr Asp 35 40 45

Tyr Cys Phe Asp Tyr Asn Pro Pro Asp Glu Asn Gln Ile Val Gly His 50 60

Gln Val Ile Leu Tyr Leu Cys His Gly Met Gly Gln Asn Gln Phe Phe 65 70 75 80

Glu Tyr Thr Ser Gln Lys Glu Ile Arg Tyr Asn Thr His Gln Pro Glu 85 90 95

Gly Cys Ile Ala Val Glu Ala Gly Met Asp Thr Leu Ile Met His Leu $100 \hspace{1cm} 105 \hspace{1cm} 110$

Cys Glu Glu Thr Ala Pro Glu Asn Gln Lys Phe Ile Leu Gln Glu Asp 115 120 125

Gly Ser Leu Phe His Glu Gln Ser Lys Lys Cys Val Gln Ala Ala Arg 130 135 140

Lys Glu Ser Ser Asp Ser Phe Val Pro Leu Leu Arg Asp Cys Thr Asn 145 150 155 160

<210> 119

<211> 173

<212> PRT

<213> Homo sapiens

Ser Asp His Gln Lys Trp Phe Phe Lys Glu Arg Met Leu 165 170

<210> 120 <211> 528 <212> DNA <213> Homo sapiens
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<400> 121
Glu Lys Pro Asp Cys Met Glu Arg Leu Gln Leu Gln Arg Arg Leu Gly 1 10 15
Cys Arg Thr Phe His Trp Phe Leu Ala Asn Val Tyr Pro Glu Leu Tyr 20 30
Pro Ser Glu Pro Arg Pro Ser Phe Ser Gly Lys Leu His Asn Thr Gly 35 40 45
Leu Gly Leu Cys Ala Asp Cys Gln Ala Glu Gly Asp Ile Leu Gly Cys 50 60
Pro Met Val Leu Ala Pro Cys Ser Asp Ser Arg Gln Gln Gln Tyr Leu 65 70 75 80
Gln His Thr Ser Arg Lys Glu Ile His Phe Gly Ser Pro Gln His Leu 85 90 95
Cys Phe Ala Val Arg Gln Glu Gln Val Ile Leu Gln Asn Cys Thr Glu 100 105 110

Glu Gly Leu Ala Ile His Gln Gln His Trp Asp Phe Gln Glu Asn Gly 115 120 125

Met Ile Val His Ile Leu Ser Gly Lys Cys Met Glu Ala Val Val Gln 130 135 140

Glu Asn Asn Lys Asp Leu Tyr Leu Arg Pro Cys Asp Gly Lys Ala Arg 145 150 155 160

Gln Gln Trp Arg Phe Asp Gln Ile Asn Ala Val Asp Glu Arg 165 170

<210> 122

<211> 498

<212> DNA

<213> Homo sapiens

<400> 122

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<400> 123

Tyr Gly Asp Val Ser Val Arg Lys Thr Leu Arg Glu Asn Leu Lys Cys
1 10 15

Lys Pro Phe Ser Trp Tyr Leu Glu Asn Ile Tyr Pro Asp Ser Gln Ile 20 25 30

Pro Arg Arg Tyr Tyr Ser Leu Gly Glu Ile Arg Asn Val Glu Thr Asn $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$

Gln Cys Leu Asp Asn Met Gly Arg Lys Glu Asn Glu Lys Val Gly Ile 50 55 60

<210> 123

<211> 165

<212> PRT

<213> Homo sapiens

Phe Asn Cys His Gly Met Gly Gly Asn Gln Val Phe Ser Tyr Thr Ala 65 70 75 80 Asp Lys Glu Ile Arg Thr Asp Asp Leu Cys Leu Asp Val Ser Arg Leu 85 90 95 Asn Gly Pro Val Ile Met Leu Lys Cys His His Met Arg Gly Asn Gln 100 105 110 Leu Trp Glu Tyr Asp Ala Glu Arg Leu Thr Leu Arg His Val Asn Ser Asn Gln Cys Leu Asp Glu Pro Ser Glu Glu Asp Lys Met Val Pro Thr Met Gln Asp Cys Ser Gly Ser Arg Ser Gln Gln Trp Leu Leu Arg Asn 145 150 155 160 Met Thr Leu Gly Thr <210> 124 516 <211> <212> DNA <213> Homo sapiens <400> 124 tcgggaatgt tgagagcaga ttggacctga ggaagaatct gcgctgccag agcttcaagt 60 120 ggtacctgga gaatatctac cctgaactca gcatccccaa ggagtcctcc atccagaagg 180 gcaatatccg acagagacag aagtgcctgg aatctcaaag gcagaacaac caagaaaccc caaacctaaa gttgagcccc tgtgccaagg tcaaaggcga agatgcaaag tcccaggtat 240 300 gggccttcac atacacccag aagatcctcc aggaggagct gtgcctgtca gtcatcacct tgttccctgg cgccccagtg gttcttgtcc tttgcaagaa tggagatgac cgacagcaat 360 ggaccaaaac tggttcccac atcgagcaca tagcatccca cctctgcctc gatacagata 420 480 tgttcggtga tggcaccgag aacggcaagg aaatcggcgt caacccatgt gagtcctcac tcatgagcca gcactgggac atggtgagtt cttgag 516 <210> 125 171 **PRT** Homo sapiens <400> 125 Phe Gly Asn Val Glu Ser Arg Leu Asp Leu Arg Lys Asn Leu Arg Cys
1 10 15

Gln Ser Phe Lys Trp Tyr Leu Glu Asn Ile Tyr Pro Glu Leu Ser Ile 20 25 30 Pro Lys Glu Ser Ser Ile Gln Lys Gly Asn Ile Arg Gln Arg Gln Lys 35 40 45 Cys Leu Glu Ser Gln Arg Gln Asn Asn Gln Glu Thr Pro Asn Leu Lys 50 60 Leu Ser Pro Cys Ala Lys Val Lys Gly Glu Asp Ala Lys Ser Gln Val 65 70 75 80 Trp Ala Phe Thr Tyr Thr Gln Lys Ile Leu Gln Glu Glu Leu Cys Leu 85 90 95 Ser Val Ile Thr Leu Phe Pro Gly Ala Pro Val Val Leu Val Leu Cys 100 105 110 Lys Asn Gly Asp Asp Arg Gln Gln Trp Thr Lys Thr Gly Ser His Il<u>e</u> 115 120 125 Glu His Ile Ala Ser His Leu Cys Leu Asp Thr Asp Met Phe Gly Asp 130 140 Gly Thr Glu Asn Gly Lys Glu Ile Gly Val Asn Pro Cys Glu Ser Ser 145 150 155 160 Leu Met Ser Gln His Trp Asp Met Val Ser Ser 165 170 <210> 126 492 DNA Homo sapiens <400> 126 agtgtggcta cgcggataga gcagaggaag aagatgaact gcaagtcctt ccgctggtac 60 120 ctggagaacg tctacccaga gctcacggtc cccgtgaagg aagcactccc cggcatcatt aagcaggggg tgaactgctt agaatctcag ggccagaaca cagctggtga cttcctgctt 180 ggaatgggga tctgcagagg gtctgccaag aacccgcagc ccgcccaggc atggctgttc 240 300 agtgaccacc tcatccagca gcaggggaag tgcctggctg ccacctccac cttaatgtcc

tcccctggat ccccagtcat actgcagatg tgcaacccta gagaaggcaa gcagaaatgg

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ccacacacat ga

360

420

480

<210> 127

<211> 163

<212> PRT

<213> Homo sapiens

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Ser Val Ala Thr Arg Ile Glu Gln Arg Lys Lys Met Asn Cys Lys Ser 1 10 15

Phe Arg Trp Tyr Leu Glu Asn Val Tyr Pro Glu Leu Thr Val Pro Val 20 25 30

Lys Glu Ala Leu Pro Gly Ile Ile Lys Gln Gly Val Asn Cys Leu Glu 35 40 45

Ser Gln Gly Gln Asn Thr Ala Gly Asp Phe Leu Leu Gly Met Gly Ile 50 60

Cys Arg Gly Ser Ala Lys Asn Pro Gln Pro Ala Gln Ala Trp Leu Phe 65 70 75 80

Ser Asp His Leu Ile Gln Gln Gln Gly Lys Cys Leu Ala Ala Thr Ser 85 90 95

Thr Leu Met Ser Ser Pro Gly Ser Pro Val Ile Leu Gln Met Cys Asn 100 105 110

Pro Arg Glu Gly Lys Gln Lys Trp Arg Arg Lys Gly Ser Phe Ile Gln 115 120 125

His Ser Val Ser Gly Leu Cys Leu Glu Thr Lys Pro Ala Gln Leu Val 130 135 140

Thr Ser Lys Cys Gln Ala Asp Ala Gln Ala Gln Gln Trp Gln Leu Leu 145 150 155 160

Pro His Thr